

Pregnancy Test Explanations

Explanations

Understanding hCG:

(See below for definitions of specific terms)

When NIH scientists did their research in the early 1970s on measuring and identifying hCG, they were not sure what the role of hCG was in normal pregnancy, what normal levels of hCG should be, or how they would rise and fall during the course of the pregnancy.

Much research has been done, however, in the last 30 years, to answer these questions. Here is what happens during the menstrual cycle and pregnancy as it relates to hCG.

There are three phases of the menstrual cycle:

1. **Follicular phase:** the pituitary gland increases release of follicle stimulating hormone (FSH) and luteinizing hormone (LH). FSH stimulates growth of follicles in the ovary and prompts the release of estrogen from the ovary. Estrogen, in turn, causes the thickening of the endometrium. One follicle will mature and release an ovum (egg). LH is secreted mid-cycle, and stimulates the release of that ovum from the follicle in the ovary.
2. **Ovulatory phase:** The ovum is released from the follicle and makes its way down the fallopian tubes toward the uterus, perhaps to be fertilized along the way. There are increased levels of LH during this phase. An ovulation prediction kit will detect a surge in LH about 1-2 days before ovulation.
3. **Luteal phase:** this covers the time from ovulation through the next menstrual period. Following ovulation the follicle that released the ovum closes and becomes the corpus luteum. LH sustains the corpus luteum until, in the event of pregnancy, it is supported by hCG. Increased production of estrogen and progesterone follow. Both hormones prepare the endometrium for the implantation of a fertilized egg.



Early e.p.t test kit, courtesy Pfizer, Inc.

If pregnancy does not occur: the corpus luteum regresses, the hormone levels of progesterone and estrogen go back down, and the breakdown of the endometrium causes menstrual bleeding. The corpus luteum will last 10 to 14 days and then die.

If pregnancy does occur, the blastocyst begins to produce hCG. This hormone stimulates the corpus luteum, preventing it from dying in early pregnancy. The corpus luteum produces estrogen and progesterone in the early part of the pregnancy, and is therefore vital for maintaining that pregnancy. Later, these hormones will be produced by the placenta. Therefore, if the corpus luteum does not function early on, the uterine lining will not support a pregnancy. Menstruation will occur and the pregnancy will miscarry. hCG is produced by the placenta in pregnancy, specifically by what is called the trophoblast of the chorionic villi. Levels are higher in the first trimester and then decrease as other hormones take over the job of protecting the embryo and, later, the fetus.

If, for any reason, the embryo does not develop normally, the trophoblast will lose its capacity to sustain the rapid rise in hCG necessary to maintain the corpus luteum. To force support of the corpus luteum and sustain a pregnancy, hCG can be used clinically as part of IVF (in-vitro fertilization) and other infertility programs.

Selected terms:

- **Endocrinology:** Endocrinology is the study of the nature and effects of hormones. Reproductive endocrinology, then, is the study of hormones related to reproduction.
- **Hormone:** A hormone is a "chemical messenger" produced in the human body by the endocrine glands. The hormone then acts on a distant target organ.
- **Chorion:** the outermost protective membrane around the fetus. The life-support system for the embryo and fetus will be the chorion, amniotic fluid, the umbilical cord, and the placenta.
- **Gonadotropin:** any substance that stimulates the gonads (ovary/testes). The three main human gonadotropins are: FSH (follicle stimulating hormone), LH (luteinizing hormone), and hCG (human chorionic gonadotropin). Their functions in female reproduction are explained above in the description of the menstrual cycle. TSH (thyroid stimulating hormone) also shares biological characteristics with these hormones.
- **Corpus luteum:** a yellow glandular mass remaining in the ovary after a follicle has ruptured to release its ovum.
- **Hemagglutination:** Hemagglutination tests are based on an antigen-antibody reaction. Distilled water and urine are added to a freeze-dried mixture of hCG antiserum from rabbits and hCG-coated red blood cells from sheep. If there is no hCG in the urine, the antibodies bind to the sheep cells, resulting in clumping (or, more technically, "hemagglutination"). If there is hCG in the urine, the antibodies will bind to it, instead, causing the sheep cells to fall out of solution and forming a reddish-brown ring at the bottom of the vial. This ring is a sign of pregnancy. Hemagglutination tests were used at doctor's offices to diagnose pregnancy in the 1960s and 1970s.
- **Antigen, antibody, antiserum:** An antigen is a substance that can act on the immune system and cause the system to create antibodies against it. An antibody is made by the immune system as part of a process to destroy the antigen. An antiserum is created by scientists. It is a blood serum that contains antibodies to known antigens. Antiserums are often prepared from immunized rabbits or other animals, as was the case with the antiserum to the beta-subunit of hCG. This process is often used in the diagnosis and treatment of disease.
- **Bioassays/Immunoassays/Radioimmunoassays:** Scientists in NICHD's Reproductive Research Branch developed a radioimmunoassay in 1972 to detect and measure hCG. This was an improvement on previous bioassays and immunoassays used to detect the presence of certain hormones.
- **Bioassay:** A bioassay is a test that uses animals or live tissue to look for a response to the hormone that is injected or added.
- **Immunoassay:** An immunoassay is a test that uses antibodies directed against the hormone to "capture" the hormone. The test involves using materials or substances that are related to or are part of the immune system. To perform an immunoassay, a scientist introduces cells from the immune system with serum that may or may not have an antibody, and observes whether or not the cells clump together.
- **Radioimmunoassay:** A radioimmunoassay uses a radioisotope as the label to detect and measure the amount of hormone present in the sample.
 - **JV:** The biologic assays were too insensitive. A couple of years before I arrived here in Bethesda, [NCI researcher] Roy Hertz had developed a way of treating choriocarcinoma with chemotherapy, and in order to monitor whether they had cured the patient, they had to use bioassays, and the bioassays were not very sensitive. They are about a thousandfold less sensitive than radioimmunoassays.
 - **JV:** The first time we tried using I125 [the radioactive isotope of iodine] -- it had never been used before for labeling hormone for doing radioimmunoassay -- it worked. I just made some guesses how to do it, and it worked. It's nice when that happens. It saves a lot of grief.

Further Reading